HFI-35

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

M4241 n

19900 MacArthur Blvd., Ste 300
Irvine, California 92612-2445
Telephone (949) 798-7600

WARNING LETTER

SEP 2 2 2000

CERTIFIED MAIL – RETURN RECEIPT REQUESTED

Robert M. Kaminski
Chief Executive Officer
Leiner Health Products, Inc.
901 East 233 Street
Carson CA. 90745

W/L 77-00

Dear Mr. Kaminski:

During an inspection of your repacking and distribution facilities located at 901 East 233 Street in Carson, CA, concluded July 13, 2000, our FDA investigators documented deviations from the Current Good Manufacturing Practices (cGMPs) for Finished Pharmaceuticals (Title 21, Code of Federal Regulations, (CFR) §210 and §211). Those deviations cause all drug products manufactured at your facility to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act). The violations from 21 CFR §211 include:

1. Failure to establish and follow procedures for cleaning and maintenance of equipment [§211.67(b)]. For example, cleaning validation has not been performed for any of your packaging lines. In addition, Standard Operating Procedures (SOPs) regarding cleaning were not followed and resulted in "foreign" tablets present in product.

2. Failure to establish production and process control procedures designed to assure your drug products have the required identity, strength, quality and purity [§211.100(a)]. For example, you have neither qualified any packaging equipment nor validated the use of any packaging lines at your facility.

3. Failure to establish appropriate control over computer systems [§211.68(b)]. For example, the Commerce in Manufacturing (CIM) system has not been validated. This system is used in the maintenance of finished product warehousing and distribution.

4. Failure to establish and follow appropriate procedures describing the handling of complaints [§211.198]. For example, complaint investigations were not performed if the complainant did not return product.

5. Failure to establish and follow procedures describing in sufficient detail the storage of drug components [§211.80(a)]. For example, you have not conducted temperature and humidity mapping of your warehousing/distribution areas. Temperature is monitored using chart recorders located at eye level (approximately 6 feet above the floor). The highest level where product is stored is approximately 25 feet above the floor. In addition, the temperature and relative humidity charts are not reviewed daily as required by SOP.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your Carson, CA facilities. It is your responsibility to assure adherence with each requirement of the Good Manufacturing Practice Regulations. You should take prompt action to correct these deviations and prevent their recurrence. Failure to promptly correct these deviations may result in regulatory action without further notice. Possible actions include seizure and/or injunction. Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts. Additionally, pending Antibiotic Form 6, New Drug Applications, Abbreviated New Drug Applications or export approval requests may not be approved until the above violations are corrected.

We acknowledge the receipt of your letter dated July 31, 2000, in which you responded to the inspectional observations reported on Form FDA-483 issued at the conclusion of the inspection. Your firm has received several complaints regarding cross contamination where foreign capsules/tablets have been found in drug products. It is incumbent on your firm to act appropriately when these complaints are received. Appropriate actions should involve an investigation, and, as required under 21 CFR 211.192, the investigation should extend "to other batches of the same drug product and other drug products that may have been associated with the specific failure or discrepancy". We have no assurance that your investigations into product cross contamination are adequate nor that they have been extended to other potentially affected drug products to assure that all products repacked at your facility have the requisite identity, strength quality and purity they are represented to possess.

A warning letter issued to your Madison, WI repacking facility in December 1998 cites violations very similar in nature to the current observations regarding cleaning, line clearance and process validation. Based on our inspection, and the previous warning letter issued to your firm and addressed to you (enclosed), the District considers the lack of appropriate cleaning and line clearance a serious systemic problem that you have been unable to address. For all of the above reasons, we are asking you to contact this office to arrange a meeting with us to discuss this matter to be held within five (5) working days of receipt of this letter. Be prepared to discuss the disposition of all products repackaged by your firm currently in distribution during this meeting. You may contact the District Director's Office at 949-798-7714 to schedule this meeting.

Furthermore, you should notify this office in writing within ten (10) days following the above meeting of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective

action can not be completed within ten (10) working days, state the reason for the delay and the time within which corrections will be completed. Besides the issues that will be discussed during the above meeting, please address the following additional comments regarding your response to the FDA 483:

We were unable to assess your response to observation 1(c). Please provide more detail regarding the computer validation procedures you have committed to in your FDA-483 response. It is unclear to the District that your procedures encompass all the requirements of 21 CFR §211.68, Automatic, mechanical, and electronic equipment, and 21 CFR §11, ELECTRONIC RECORDS; ELECTRONIC SIGNATURES.

It appears you may have a conflict between two SOPs you have modified in response to observation 4. The updated version of SOP [redacted] appears to conflict with draft SOP [redacted]. Please review these SOPs for a conflict and make appropriate changes as your review indicates.

Your written response should be directed to the Food and Drug Administration, Attention:

Thomas L. Sawyer
Director, Compliance Branch
Food and Drug Administration
19900 MacArthur Blvd., Suite 300
Irvine, CA 92612

Sincerely,

Michael O. Stokke
Acting District Director

cc: California Department of Health Services, Food & Drug Branch
601 N. 7th Street
Sacramento, California 94234-7320
Attn: Stuart Richardson, Jr., Chief